American Journal of Medical Genetics 63:479–481 (1996)

Ectodermal Dysplasia, Rapp-Hodgkin Type in a Mother and Severe Ectrodactyly-Ectodermal Dysplasia-Clefting Syndrome (EEC) in Her Child

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We describe a mother with manifestations most consistent with the Rapp-Hodgkin type of ectodermal dysplasia and her malformed newborn son with ectrodactyly, ectodermal dysplasia, cleft palate, and bilateral cystic and obstructive ureteroceles with hydroureters and cystic renal dysplasia as described in the EEC syndrome.

This observation suggests that the Rapp-Hodgkin type of ectodermal dysplasia and EEC syndrome, both defined as autosomal dominant conditions with variable expression, may be manifestations of the same mutated gene. We also want to emphasize that urogenital anomaly is another hallmark of the EEC syndrome. © 1996 Wiley-Liss, Inc.

KEY WORDS: autosomal dominant inheritance, cystic renal dysplasia, EEC syndrome, Rapp-Hodgkin type of ectodermal dysplasia

INTRODUCTION

Ectodermal dysplasia, Rapp-Hodgkin type [Rapp and Hodgkin, 1968], and ectrodactyly-ectodermal dysplasia-clefting syndrome, also termed EEC syndrome [Rüdiger et al., 1970], have hitherto been classified as different autosomal dominantly inherited ectodermal dysplasia syndromes. The two syndromes present great variability in clinical expression. In individual patients, nosological classification and final diagnosis, based solely on clinical criteria, may be difficult.

Received for publication July 5, 1995; revision received December 5, 1995.

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CLINICAL REPORT

The index patient of this report, S.F., is a woman, born August 1952, as the oldest of six children. Both parents, three brothers, and two sisters are healthy and normal. Family history is unremarkable.

Pre- and perinatal histories were normal. Birthweight was 3,200 g and length was 48 cm. A cleft of the soft palate was corrected at 1 year. Psychomotor and mental development were normal. She is working as a social nurse. At the age of 29 years she requested genetic counseling. Since early childhood she was followed dermatologically for hypohidrotic ectodermal dysplasia. Weight and height were 42 kg and 148 cm, respectively. There was almost complete alopecia with sparse, uncombable, straw-like hair in the temporal and occipital region. Scanning electronmicroscopic examination showed pili canaliculi with irregular twists. There had been hypodontia and microdontia of the primary dentition and absence of all permanent teeth. Nails were dysplastic and sweating was limited except for the scalp. Eye-brows, eye-lashes, and body hair were scanty. Especially in the face the skin was thin, dry, and dystrophic; there was frontal bossing, relative maxillary hypoplasia with a small pinched nose. On her right shoulder there were two keloids, 3 cm in length, after surgical excision of two ulcer-like lesions.

Since the clinical findings were most consistent with the diagnosis of Rapp-Hodgkin type of ectodermal dysplasia, she was informed about the apparent autosomal dominant inheritance of the syndrome with variable expression.

After two failed donor IVF procedures, and because of a strong desire for childbearing, she was prepared to take the risk of a normal pregnancy. A first pregnancy ended in a first trimester spontaneous abortion. In the second pregnancy, at the age of 42 years, amniocentesis at 15 weeks of gestation documented a normal karyotype 46,XY. At 30 weeks of gestation, ultrasound examination showed oligohydramnios and bilateral renal anomalies. The infant was born at 35 weeks of gestation. Weight was 2,175 g (25th–50th centile), crown-heel length was 45.0 cm (25th–50th centile), and head circumference was 30.0 cm (10th centile).

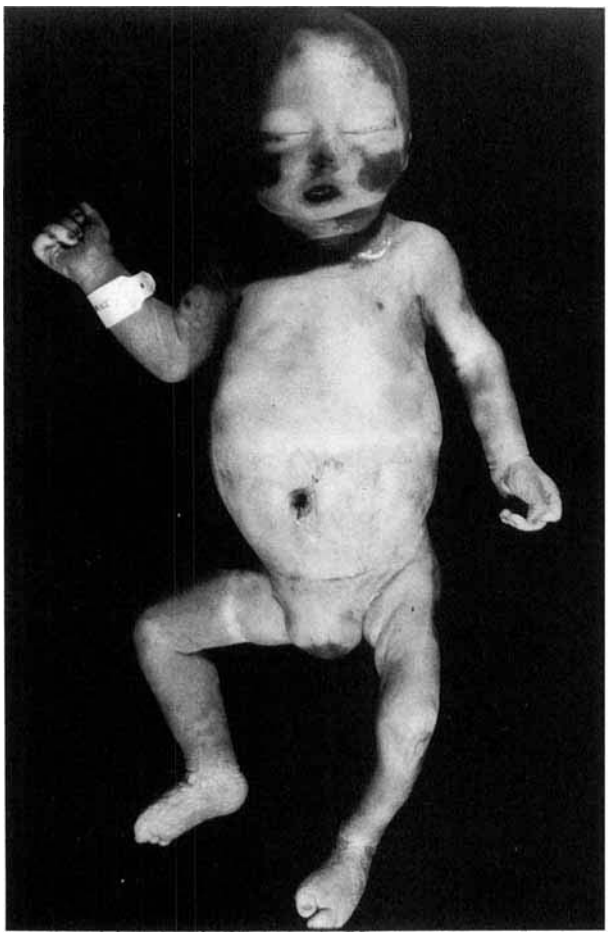

Fig. 1. Newborn boy with severe EEC syndrome.

Fig. 2. Filiform adhesions of the eyelids.

Clinical examination (Fig. 1) showed a triangular face, small, low-set auricles with adherent lobules, retrognathia, and a complete cleft of the palate. Both eyes showed several adhesions between the eyelids (Fig. 2). There was ectrodactyly of the feet with absent 2nd and 3rd toes on the right foot, absent 2nd toe on the left foot, and bilateral partial cutaneous syndactyly 3–4 (Fig. 3). The skin was dry and scaly with almost complete absence of hair. The nails were small and brittle.

The baby died September 1994, at 1 day of age. Autopsy demonstrated severe pulmonary hypoplasia. There was bilateral cystic dysplasia of the kidneys (Potter type IV) with hydroureters. These anomalies were secondary to bilateral cystic and obstructive ureteroceles (Fig. 4).

DISCUSSION

The association of ectrodactyly, ectodermal dysplasia, and cleft lip/palate, as observed in the present malformed male fetus, was first recognized by Rüdiger et al. [1970], who coined the term EEC syndrome. Ectrodactyly refers to the absence or deficiency of one or more central digits of hand or foot. Ectodermal dysplasia is variably characterized by sparse hair, small brittle nails, and absent sweat glands. Various anomalies of the kidneys and ureters have been described in EEC syndrome. Hydronephrosis, hydroureters, renal agenesis, or renal duplication occur in at least 20% of cases [Rollnick and Hoo, 1988]. Nardi et al. [1992] even found urogenital anomalies in 13 out of 25 (52%) patients, indicating that urogenital anomaly aside from ectrodactyly is also a hallmark of EEC syndrome. In our case, autopsy documented bilateral cystic and obstructive ureteroceles with hydroureters and cystic renal dysplasia. These anomalies gave rise to the Potter oligohydramnios sequence with pulmonary hypoplasia as the cause of neonatal death. Many cases of EEC syndrome are sporadic. However, several reported families showed an autosomal dominant mode of inheritance with incomplete penetrance and variable expression [Pfeiffer and Verbeck, 1973; Penchaszadeh and de-Negrotti, 1976; Rosenmann et al., 1976; Opitz et al., 1980]. Heterogeneity may exist.

Ectodermal dysplasia and clefts of the lip and palate are also major findings of the Rapp-Hodgkin type of ectodermal dysplasia [Rapp and Hodgkin, 1968; Wannarachue et al., 1972]. This syndrome is an autosomal dominant trait with variable expression and includes

Fig. 3. Left foot, showing absent second toe and cutaneous syndactyly 3–4. Note also the dry and scaly skin.

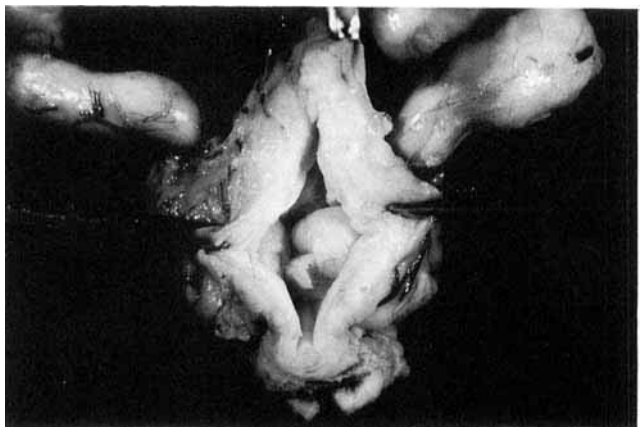

Fig. 4. Opened urinary bladder with cystic ureteroceles. Bilateral hydroureters.

hypospadias in males. Short stature is another hallmark of Rapp-Hodgkin syndrome. The clinical findings and symptoms of the mother (short stature, hypohidrotic ectodermal dysplasia, cleft palate, pili canaliculi, and twists of hairs on scanning electronmicroscopy) were most compatible with this diagnosis. Our observation of EEC syndrome in a newborn boy and ectodermal dysplasia of the Rapp-Hodgkin type in the mother is unique and indicates that these two forms of ectodermal dysplasia may be variable manifestations of the same mutation.

An additional finding in the present case is the presence of filiform adhesions of the eyelids, or so-called "ankyloblepharon filiforme adnatum." Interestingly, the association of cleft lip with or without cleft palate and congenital filiform fusion of the eyelids has also been described as an autosomal dominant trait with extremely variable expression [Rogers, 1961; Long and Blandford, 1962]. Hay and Wells [1976] described seven patients from four families with autosomal dominant inheritance of congenital ankyloblepharon, ectodermal defects, and cleft lip and palate (AEC syndrome).

The present observation illustrates once more the great difficulty in genetic counseling of ectodermal dysplasias, due to the great variability in expression of the different syndromic forms, and the great clinical overlap between the different conditions.

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